Clopidogrel (Plavix®) Criteria for Use in Veteran Patients

VHA Pharmacy Benefits Management Strategic Healthcare Group and the Medical Advisory Panel

The following recommendations are based on current medical evidence and expert opinion from clinicians. The content of the document is dynamic and will be revised as new clinical data becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. The clinician, however, must make the ultimate judgment regarding the propriety of any course of treatment in light of individual patient situations.

Recommendations for use of clopidogrel in acute coronary syndrome/unstable angina

- Clopidogrel should be administered to hospitalized patients who are unable to take aspirin due to gastrointestinal intolerance or hypersensitivity. (Level of Evidence A)
- In patients hospitalized for acute coronary syndrome/unstable angina in whom no revascularization procedure is planned, clopidogrel should be added to aspirin as soon as possible for at least 1 month (Level of Evidence A) and up to 9 months (Level of Evidence B). The number needed to treat for a benefit was 1:50 from the CURE trial.
- Addition of subcutaneous LMWH or intravenous UFH to the regimen of clopidogrel and/or aspirin should be considered. (Level of Evidence A)
- There is insufficient evidence to recommend initiation of clopidogrel in stable outpatients who experienced an episode of ACS/unstable angina in the past.
- If clopidogrel is to be initiated in an outpatient, an angiogram should have been performed to evaluate for any surgical interventions. (Level of Evidence B)
- The risk of bleeding was raised in patients who received clopidogrel during the CURE trial. The rate of major bleeds (defined as those requiring transfusion of 2 units or more) results in a number needed to treat to harm of 1:100. (Level of Evidence A)

Recommendations for use of clopidogrel post PTCA/stent

- In patients with planned cardiac intervention, clopidogrel should be initiated and continued for at least 1 month and up to 12 months. (Level of Evidence A)
- Clopidogrel was combined with aspirin therapy in the clinical trials. To achieve the response seen in these trials aspirin should be used at a dose of 81-325 mg daily. (Level of Evidence A)

Recommendations for use of clopidogrel in aspirin intolerant patients

- Clopidogrel should be used in patients who are aspirin allergic or experience major gastrointestinal intolerance. (Level of Evidence A)
- There is a relative contraindication to using clopidogrel in patient s who developed ticlopidine hypersensitivity due to a cross reactivity between agents.

Recommendations for the use of clopidogrel in recurrent ischemic events

For a discussion of the use of clopidogrel with cerebrovascular disease, please go to the VA Pharmacy Benefits Management website http://www.vapbm.org/PBM/criteria.htm and look at the criteria for use document, Pharmaceutical Selection of Antiplatelet Therapy in Cerebrovascular Disease.

Cost Comparison of Antiplatelet agents

Agent	FSS price/tablet	Tablets/day	Cost/day
Aspirin 325 mg	$0.007	1	$0.007
Aspirin 81 mg	$0.004	1	$0.004
Clopidogrel 75 mg	$2.03	1	$2.03
ASA/dipyridamole 25mg/200mg	$0.80	2	$1.60

References

1. Mitka M. Results of CURE trial for acute coronary syndrome. JAMA. 285(14):1828-9, 2001 Apr 11.
2. The Clopidogrel in Unstable Angina to Prevent recurrent Events Trial Investigators. Effects of Clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. N Engl J Med 2001;345(7):494-502.
3. Mehta SR, Yusuf S, Peters RJG, et al. Effects of pretreatment with clopidogrel and aspirin followed by long term therapy in patients undergoing percutaneous coronary intervention: the PCI-CURE study. Lancet. 2001 Aug 18;358(9281):527-33.
4. ACC/AHA Guideline Update for the Management of Patients with Unstable Angina and Non-ST-Segement Elevation Myocardial Infarction. March 2002.
5. Steinhubl SR, Berger PB, Mann JT, et al. Early and sustained dual oral antiplatelet therapy following percutaneous coronary intervention. JAMA. 2002; 288(19):2411-2420.
6. Yusuf S, Mehts SR, Zhaao F, et al. Early and late effects of clopidogrel in patients with acute coronary syndrome. Circulation. 2003;107:966-972.

Criteria Checklist for Clopidogrel

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Indication for therapy	***Response***
Patient with one of the following conditions: ❑ Outpatient with unstable angina and non ST elevation acute MI within past 3 months ❑ Post PTCA/stent placement within past month ❑ Hospitalized patient with unstable angina and non ST elevation acute MI, prior to heart catheterization ❑ Recurrent cerebrovascular ischemic events while on aspirin therapy (see http://www.vapbm.org/PBM/criteria.htm and look at the criteria for use document, Pharmaceutical Selection of Antiplatelet Therapy in Cerebrovascular Disease) ❑ Documented aspirin intolerant patient who requires antiplatelet therapy	❑ yes ❑ no ***If no, patient is ineligible to receive clopidogrel***
Duration of therapy	
❑ 1 month-post stent placement ❑ 3 months- post ACS ❑ 9 months- high risk post ACS ❑ 12 month- post stent placement ❑ indefinite- aspirin intolerant patient ❑ indefinite- cerebrovascular disease ❑ other _____	
Dosing	
❑ ACS- 300 mg load orally then daily dose of 75 mg ❑ Post stent placement-300 mg load orally then daily dose of 75 mg ❑ Non acute conditions- 75 mg daily ❑ May be given with aspirin (81-325 mg) unless aspirin is contraindicated or not tolerated. Addition of LMWH or intravenous UFH during the early phase of acute coronary syndrome/unstable angina should be considered.	
Monitoring	
❑ Patients started in-house should be monitored by cardiology ❑ Out-patients should have a cardiology referral for indefinite ACS use or longer than 3 month occurrence of ACS ❑ Patients with cerebrovascular disease should have a neurology referral if clopidogrel and aspirin are used together ❑ Patients should be followed for development of neutropenia or thrombotic thrombocytopenic purpura	
Contraindications	
Any of the following: ❑ Active bleeding ❑ High risk of bleeding ❑ History of bleeding diathesis ❑ Patient with chest pain without EKG changes in whom etiology of chest pain is unlikely to be ischemic in origin ❑ Known hypersensitivity to ticlopidine, due to cross reactivity or any component of the product ❑ Known hypersensitivity to clopidogrel or any component of the product	❑ yes ❑ no ***If yes, patient is ineligible to receive clopidogrel***

Approved by Physician: _____ Date/time: _____

Patient name (last 4): _____ Reviewer: _____

Length of therapy _____approved_____